

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP2004/010879

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 G01N33/68 G01N33/94

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>CLEUTJENS JACK P M ET AL: "Thrombospondin 2 deficiency in mice results in cardiac rupture early after myocardial infarction" CIRCULATION, vol. 100, no. 18 SUPPL., 2 November 1999 (1999-11-02), page I.56, XP009027984</p> <p>72nd Scientific Sessions of the American Heart Association; Atlanta, Georgia, USA; November 7-10, 1999</p> <p>ISSN: 0009-7322</p> <p>abstract</p> <p>-----</p> <p>-/-</p>	7-10,12
Y		1

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

## \* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the International filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the International filing date but later than the priority date claimed

\*T\* later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&\* document member of the same patent family

Date of the actual completion of the international search

19 November 2004

Date of mailing of the International search report

25/11/2004

Name and mailing address of the ISA  
European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel: (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Bigot-Maucher, C

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT /EP2004/010879

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TOPOL ERIC J ET AL: "Single nucleotide polymorphisms in multiple novel thrombospondin genes may be associated with familial premature myocardial infarction" CIRCULATION, vol. 104, no. 22, 27 November 2001 (2001-11-27), pages 2641-2644, XP001180429 ISSN: 0009-7322 page 2642, column 1, paragraph 4	7-10,12
Y	SHIRAKATA Y ET AL: "Inverse regulation of the angiogenesis factor VEGF and the angiogenesis inhibitors thrombospondin-1 and TSP-2 in human epidermal keratinocytes" JOURNAL OF INVESTIGATIVE DERMATOLOGY, vol. 117, no. 2, August 2001 (2001-08), page 391, XP001180423 62nd Annual Meeting of the Society for Investigative Dermatology; Washington, DC, USA; May 09-12, 2001 ISSN: 0022-202X abstract	1-6
X	GIORDANENGO L ET AL: "Anti-galectin-1 autoantibodies in human Trypanosoma cruzi infection: Differential expression of this beta-galactoside-binding protein in cardiac Chagas' disease" CLINICAL AND EXPERIMENTAL IMMUNOLOGY, vol. 124, no. 2, May 2001 (2001-05), pages 266-273, XP009028059 ISSN: 0009-9104 page 267, column 2, paragraph 4	7-10
Y	abstract	1-6,11
Y	MATTHEWS KENNETH P ET AL: "Evidence for IgG autoantibodies to galectin-3, a beta-galactoside-binding lectin (Mac-2, epsilon binding protein, or carbohydrate binding protein 35) in human serum" JOURNAL OF CLINICAL IMMUNOLOGY, vol. 15, no. 6, 1995, pages 329-337, XP009027994 ISSN: 0271-9142 abstract page 331, column 1, last paragraph	1-6,11
	-/-	

## INTERNATIONAL SEARCH REPORT

International Application No PCT /EP2004/010879
--

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
T	<p>SCHROEN BLANCHE ET AL: "Genomic analysis identifies thrombospondin-2 as a molecular predictor of heart failure."</p> <p>CIRCULATION, vol. 108, no. 17 Supplement, 28 October 2003 (2003-10-28), pages IV-260, XP009027986</p> <p>American Heart Association Scientific Sessions 2003;Orlando, FL, USA; November 09-12, 2003</p> <p>ISSN: 0009-7322 (ISSN print) abstract</p> <p>-----</p>	1-12
T	<p>SHARMA UMESH C ET AL: "Galectin-3 is a novel macrophage derived mediator of cardiac fibrosis and specifically marks failing hearts."</p> <p>CIRCULATION, vol. 108, no. 17 Supplement, 28 October 2003 (2003-10-28), pages IV-261, XP009027985</p> <p>American Heart Association Scientific Sessions 2003;Orlando, FL, USA; November 09-12, 2003</p> <p>ISSN: 0009-7322 (ISSN print) abstract</p> <p>-----</p>	1-12
T	<p>WALTON BRIAN ET AL: "Thrombospondin-2 and lymphotoxin-alpha gene variations predict coronary heart disease in a large prospective study."</p> <p>CIRCULATION, vol. 108, no. 17 Supplement, 28 October 2003 (2003-10-28), pages IV-771, XP009027983</p> <p>American Heart Association Scientific Sessions 2003;Orlando, FL, USA; November 09-12, 2003</p> <p>ISSN: 0009-7322 (ISSN print) abstract</p> <p>-----</p>	1-12

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP2004/010879

### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  
Although claim(s) 7-10 are directed to a diagnostic method practised on the human/animal body (Article 52(4) EPC), the search has been carried out and based on the alleged effects of the compound/composition.
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple Inventions in this International application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claim(s) 7-10 are directed to a diagnostic method practised on the human/animal body (Article 52(4) EPC), the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box II.2

Claims Nos.: -

Present claims 1-12 relate to an extremely large number of possible compounds/products/methods due to the broad term "non-myocytical marker". The same is true for claims 11-12 due to the term "modulators thereof". Support within the meaning of Article 84 EPC and/or disclosure within the meaning of Article 83 EPC is to be found, however, for only a very small proportion of the compounds/products/methods claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds/products/methods relating to thrombospondin-2 and galectin-3 (see p 5, para 1 to p 6, para 1; examples).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.